REMARKS

Claims 22-25 are pending in this application. Claims 22-25 have been canceled. Claims 28-31 have been added. No new matter has been added by this amendment. Reconsideration is respectfully requested.

I. Specification Informalities

The Examiner has objected to the disclosure for the use of the abbreviations SarR and SarA. The Examiner has requested that the full name and description of these abbreviations be recited when they appear for the first time in the specification.

The use of the trademarks has been noted in this application (i.e. FACscan and MonoQ). The Examiner suggests that it should be capitalized wherever it appears and be accompanied by the generic terminology. Appropriate corrections have been requested.

In accordance with the Examiner's suggestions the specification has been amended as reflected above to include a description of Sar R and Sar A as staphylococcal accessory regulatory proteins (on pages 2 and 3 of the specification), and further to capitalize the trademarks FACscan and MonoQ (on pages 22 and 26 of the specification), and include the generic terminology. Further, the specification has been amended on page 1 at line 10 to correct a typographical error, namely to correctly recite *Staphylococcus aureus.*

Removal of these objections is respectfully requested.

II. Rejection of Claims under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 22-25 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. It is suggested that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed had possession of the invention. The Examiner has acknowledged the specification is enabled for a method of screening for lead compounds which inhibit the expression of virulence determinants in *Staphylococcus* species. It is suggested that the specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected to make and/or use the invention commensurate in scope with these claims.

Applicants respectfully traverse this rejection.

In an earnest effort to facilitate prosecution of this case, Applicants have canceled claims 22-25 and added new claims 28-31 drawn to methods of screening for lead compounds which inhibit the expression of virulence determinants in *Staphylococcus* species. Support for this amendment is found throughout the application and at page 5, beginning at line 4.

Accordingly, withdrawal of this rejection under 35 U.S.C. § 112, second paragraph is respectfully requested.

III. Rejection of Claims under 35 U.S.C. §112, first paragraph

The Examiner has rejected claims 22-25 under 35 U.S.C. §112, first paragraph, as failing to comply with the written

description requirement. It is suggested that the specification at pages 20-22 recites bacterial strains and plasmids which have been used for the completion of the instant invention. However, the specification is suggested to lacks complete deposit information for the deposit of these strains, especially RN6390. The Examiner suggests that it is unclear if the *S.aureus* strain possessing the properties of RN6390 and others are known and publically available or can be reproducibly isolated from nature without undue experimentation. The Examiner has required a suitable deposit for patent purposes.

Applicants respectfully traverse this rejection.

The protypical SarA strain RN6390 is clearly accessible to those of skill in the art as witnessed by numerous studies being performed on the strain and identifiable via internet search for the key words/term "RN6390". As is further, evidenced by the U.S. Patent 5,976,792 issued November 2, 1999, the nucleotide sequence of sar A of S.aureus strain RN6390, is clearly set forth as SEQ ID NO:11, at column 4, paragraph 2, and at Figure 4. Thus, as required by MPEP 2404.02, one of skill would be able to routinely be able to practice the invention as claimed. Applicants believe that they have adequately established that the biological material is known and readily available and that no deposit is required.

Withdrawal of this rejection therefore is respectfully requested.

IV. Rejection of Claims under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 22-25 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to point out

and distinctly claim the subject matter which applicant regards as the invention. The Examiner suggests that claims 22 and 23 are incomplete for omitting essential steps of (a) how the lead compound is identified and (b) how the heterodimers are formed. The Examiner further suggests that claims 22 and 23 lack antecedent basis for the limitation "the expression of virulence". Further, it is suggested that the recitation of the phrase "sufficient to allow" is unclear, and that the abbreviations Sar A and Sar R require full name and description where they appear first. Finally, it is suggested that the term "capable" in claim 25 is a relative term which renders the term indefinite.

Applicants respectfully traverse this rejection.

In an earnest effort to advance the prosecution of this application, claims 22-25 have been canceled and new claims 28-31 have been added to address the Examiner's concerns and clarify the essential steps of the assays of the invention. In particular, claim 28 now recites that a lead compound is identified by obtaining one or more SarR analogs; contacting said one or more analogs of SarR with a SarA protein; and determining whether said one or more analogs form a heterodimer with the SarA protein wherein the formation of a heterodimer is indicative of a lead compound which inhibits the expression of virulence determinants in *Staphylococcus*. Support for a method in accordance with newly added claim 28 can be found throughout the application and in particular at page 11, line 21 to page 13, line 29 which teach that one or more SarR analogs can be obtained, for example, from chemical libraries, phage display libraries, and rationale design via computer modeling. Further,

these pages teach that one or more analogs of SarR can be, for example, contacted with a SarA protein by binding/elution experiments (see page 12, lines 22-25). Moreover page 10, lines 17-21, in view of the teachings of the application as a whole, discloses that the interference of a SarA homodimer, which positively regulates SarA expression, by a SarR/SarA heterodimer would result in a reduction in SarA expression and accordingly a loss in expression of virulence determinants.

Further, newly added claim 29 now recites that a lead compound is identified by obtaining one or more SarR analogs; contacting said one or more analogs of SarR with a SarA promoter or fragment thereof; and determining whether said one or more analogs bind the SarA promoter or fragment thereof wherein the binding of the SarR analog to the SarA promoter or fragment thereof is indicative of a lead compound which inhibits the expression of virulence determinants in *Staphylococcus*. Support for a method in accordance with newly added claim 29 can be found in claim 23 as originally filed and throughout the description and examples. In particular, page 11, line 21 to page 13, line 29 teach that one or more SarR analogs can be obtained, for example, from chemical libraries, phage display libraries, and rationale design via computer modeling. Support for the steps of contacting one or more analogs of SarR with a SarA promoter or fragment thereof and determining whether said one or more analogs bind the SarA promoter or fragment thereof is found at page 10, lines 14-16 and at pages 26-28 under the heading "Binding of SarR to *sarA* promoter fragments by gel shift and footprinting assays" which teach that binding sites in the SarA promoter system enable SarR to repress expression of SarA and the delineation of fragments of

the SarA promoter which bind SarR, respectively. Thus, as disclosed throughout the specification and in claim 23 as originally filed, SarR analogs which bind the SarA promoter are useful as lead compounds for inhibiting the expression of virulence determinants.

With regard to the limitation "the expression of virulence" in claims 22 and 23, it is respectfully pointed out that this term is recited in the preamble of the claims. However, newly added claims 28 and 29 clarify the invention and respectively recite that the formation of a SarA/SarR analog heterodimer or binding of the SarR analog to the SarA promoter, or fragment thereof, is indicative of a lead compound which inhibits the expression of virulence determinants in *Staphylococcus*. Support for this amendment is found throughout the specification and particularly at page 10, lines 17-21 and in claim 23 as originally filed.

With regard to the limitation "sufficient to allow", the Applicants respectfully assert that one of skill in the art would readily understand in light of the specification that the heterodimer between the SarA and SarR protein is formed via a bond which is sufficient to: (a) allow the formation of the heterodimer and (b) to allow the heterodimer to compete with the SarA homodimer to inhibit expression of virulence determinants. However, in an earnest effort to clarify the invention, newly added claims 28 and 29 have the term "sufficient to" deleted.

To further clarify the invention, newly added claims 28 and 29, in accordance with the Examiner's suggestions, recite the full text of *Staphylococcal accessory regulatory A* and *R* proteins in relation to the abbreviations *SarA* and *SarR*.

Moreover, in accordance with the Examiner's suggestions and in an earnest attempt to more clearly define the invention, newly added claim 31 (formerly claim 25) does not recite the term "capable".

Reconsideration and withdrawal of these rejections is respectfully requested.

V. Rejection of Claim 22-25 under 35 U.S.C. §102

Claims 22-25 are rejected under 35 U.S.C. §102 as being anticipated by Cheung et al (U.S. Patent No.5,976,792).

The Examiner suggests that Cheung et al. disclose a method of screening for lead compounds, which inhibit the expression of virulence determinants in a gram positive bacteria comprising identifying chemical entities having similarities to SarA protein. It is further suggested that Cheung et al. teach SarA and analogs including pharmaceutical compositions; disclose Sar proteins and the genes encoding such proteins; and teach Sar R and A mutants.

Applicants respectfully traverse this rejection.

Cheung et al. disclose SarA through cloning and sequencing activities (see column 12). Cheung et al. do not teach SarR protein or activity thereof. More importantly, Cheung et al. do not teach that lead compounds comprise SarR analogs, nor that such compounds inhibit the expression of virulence determinants in *Staphylococcus* species. Further, Cheung et al. do not teach or suggest that SarR analogs can form heterodimers with SarA protein and inhibit the expression of virulence determinants. Moreover, Cheung et al. do not teach that SarR analogs bind to a SarA promoter or fragment thereof.

Thus, Cheung et al. does not teach all of the limitations of the claimed instant invention, and does not anticipate the present invention.

Withdrawal of this rejection is respectfully requested.

VI. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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Date: **July 7, 2004**

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